67. (New) The baculovirus vector of Claim 66, wherein said glycosylphosphatidylinositol coding sequence is a CD59 or a CD14 gene.

68. (New) A baculovirus vector comprising a promoter and a synthetic nucleotide sequence comprising SEQ ID NO:7.

REMARKS

Upon entry of the foregoing amendment, Claims 46-53, 55-63 and 65-68 are active in the present application. Support for the amendment to Claim 46 is found on page 12, lines 24-28, and page 15 of the specification as originally filed. Support for Claims 65-68 is found in Claims 46-53, page 12, lines 24-28. Applicants have amended the specification to include the full Depository information. No new matter is believed to be added by these amendments. Favorable reconsideration is respectfully requested.

The rejection of the specification in Claims 46-64 under 35 U.S.C. §112, first paragraph, is respectfully traversed.

Claim 46 is amended to recite a signal peptide from an MSP-1 protein. With respect to the "synthetic polynucleotide encoding a 19 kilodalton C-terminal fragment of a *Plasmodium falciparum* MSP-1 protein" the Examiner has maintained that only the deposited baculovirus vectors are enabled by the present specification. Applicants respectfully disagree and note that the criteria for enablement under 35 U.S.C. §112, first paragraph, is whether the skilled artisan can practice the claimed invention without undue experimentation provided with the specification and the knowledge available in the art at the time the application was filed. Applicants submit that these criteria have been met by the present application.

Applicants respectfully direct the Examiner's attention to *Ex parte* Formal, 230 U.S.P.Q 546, 547 (Bd. Pat. App Int. 1986) which outlines the criteria for determining whether some experimentation is considered undue experimentation:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention.

Applicants also direct Examiner's attention to decision in Fields v. Conover, 443 F. 2d 1386, 170 U.S.P.Q. 276 (CCPA 1971) where the court stated that experimentation should not require ingenuity beyond that to be expected of the ordinary person skilled in the art.

The specification provides specific teaching to construct baculovirus vectors comprising a promoter and a synthetic polynucleotide encoding a 19 kilodalton C-terminal fragment of *Plasmodium falciparum* MSP-1 protein and a polynucleotide coding a signal peptide which is also from an MSP-1 protein. Screening for additional *Plasmodium falciparum* MSP-1 encoding polynucleotides and methods of mutagenesis are well-known in the art, see, for example, Sambrook et al, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York (1989).

Thus, the specification teaches not only how to construct the claimed baculovirus vector and the nucleotide sequence which encodes MSP-1, the specification teaches that a limited number of changes can be made to the nucleotide sequence of *Plasmodium falciparum*, see Figure 1A. Furthermore, the relative skill in the art is high, methods of altering the coding sequence of MSP-1 are routine and coupled with the specification would not require the skilled artisan to exert any ingenuity in making and using the claimed baculovirus vectors.

In view of the foregoing, Applicants submit that the instant claims are enabled by the the specification and as such, withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 52 and 62 under 35 U.S.C. §112, first paragraph, is believed to have been obviated by amendment.

Claim 52 is amended to depend from Claim 46 and recites that SEQ ID NO:9 is the synthetic polynucleotide. Claim 46 is amended to recite a polynucleotide encoding a signal peptide. Claim 62 is amended to depend from Claim 56, which recites a synthetic polynucleotide. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 47, 50, 52 and 55 under 35 U.S.C. §112, first paragraph, is respectfully traversed.

The specification at page 30 has been amended to include the complete Depository information and the dates the deposited materials were deposited. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 49, 53 and 56-64 under 35 U.S.C. §112, second paragraph, is believed to have been obviated by amendment.

The rejection of Claims 46, 48, 51, 54, 56, 58, 61 and 64 under 35 U.S.C. §102(b) over Longacre et al in light of the instant disclosure is respectfully traversed.

Claim 46 has been amended to recite "*Plasmodium falciparum* MSP-1 protein" and submit that such synthetic polynucleotide encoding said protein is not anticipated by Longacre et al because Longacre et al merely discloses a recombinant baculovirus containing a DNA fragment of *Plasmodium vivax* MSP-1. However, the *Plasmodium falciparum* MSP-1 in the instant claims and the Longacre et al *Plasmodium vivax* MSP-1 are not the same (see, Applicants' Amendment and Request for Reconsideration filed August 3, 2000 and the Dr.

Longacre-Andre Declaration) Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of Claims 46, 48, 51, 54-56, 58, 61 and 64 under 35 U.S.C. §103(a) over Chappel et al, Miller et al and Longacre et al is respectfully traversed.

Irrelevant disclosures of the cited references have been addressed previously. See Applicants' Amendment and Request for Reconsideration filed August 3, 2000. It is submitted that the combined teachings of the cited prior art references do not suggest altering the nucleotide sequence of the 19 kilodalton C-terminal fragment of a *Plasmodium falciparum* MSP-1 protein such that the total GC content is between 40% and 60%. Furthermore, there is no teaching in any of the cited references of why a skilled artisan would be motivated to change the nucleotide sequence of the 19 kilodalton C-terminal fragment of *Plasmodium falciparum* MSP-1 protein. As such, Applicants submit that the cited references fail to support a *prima facie* case of obviousness.

In any case, even a *prima facie* case is rebutted by Applicants' showing already of record in the Dr. Longacre-Andre Declaration. The Declaration clearly demonstrate that the protein encoded by the synthetic gene of a *Plasmodium falciparum* having a GC content of 40 to 60% exhibited significantly more reactivity with hyperimmune antiserum than the native gene which did not meet this criteria. Contrary to the Examiner's assertion that the Applicants have not shown that altering the GC content of the MSP-1 protein supports unexpected results (referring to the Examiner's statements found on pages 6-7 of the Office Action) Applicants have already shown how altering the GC content of the *Plasmodium falciparum* MSP-1 protein facilitates enhanced hyperimmune reactivity which is not suggested nor could have been expected from the combination of the cited documents. Applicants respectfully request withdrawal of this ground of rejection.

Applicants submit that the present application now stands in condition for allowance.

Early notification of such allowance is earnestly solicited.

Respectfully submitted,
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Marked-Up Copy
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Amendment Filed on:
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IN THE SPECIFICATION

Page 30, line 8, please replace the paragraph with the following:

--The microorganisms identified below have been deposited under Rule 6.1 of the Treaty of Budapest of 1st February 1996, in the Collection Nationale de Cultures de Microorganisms (C.N.C.M.) of Institut Pasteur at 28, rv du Dr. Roux 75724, Paris Cedex 15 under the following registration numbers:

Identification reference	Date of Deposit	Registration numbers
PvMSP1p19A	February 1, 1996	I-1659
PvMSP1p19S	February 1, 1996	I-1660
PfMSP1p19A	February 1, 1996	I-1661
PfMSP1p19S	February 1, 1996	I-1662
PcMSP1p19S	February 1, 1996	I-1663
G17-20 Hybridoma	February 14, 1997	I-1846--

IN THE CLAIMS

--46. (Amended) A baculovirus vector comprising a promoter, a synthetic polynucleotide encoding a 19 kilodalton C-terminal fragment of a *Plasmodium falciparum* MSP-1 protein; and wherein said synthetic polynucleotide has a GC content of 40 to 60% and a polynucleotide encoding a signal peptide wherein said signal peptide is from an MSP-1 protein.

47. (Amended) The baculovirus vector of Claim 46, wherein said synthetic polynucleotide is SEQ ID NO:1 [or SEQ ID NO:7].

49. (Amended) The baculovirus vector of Claim 48, wherein said glycosylphosphatidylinositol coding sequence is from a CD59 or CD14 gene.

51. (Amended) The baculovirus vector of Claim 46, wherein said synthetic polynucleotide [further comprises a] and said polynucleotide encoding a signal peptide comprises SEQ ID NO:7.

52. (Amended) The baculovirus vector of Claim 46 [51], wherein said synthetic polynucleotide is SEQ ID NO:9.

53. (Amended) The baculovirus vector of Claim 46, wherein said synthetic polynucleotide further comprises a polynucleotide encoding [the] a *Plasmodium vivax* Duffy binding protein or [the] a *Plasmodium falciparum* EBA-175 protein.

Claim 54 (Cancelled).

55. (Amended) [The] A baculovirus vector [of Claim 46] selected from the group consisting of PfMSP1p19A, PfMSP1p19S, and PcMSP1p19S.

56. (Amended) A synthetic polynucleotide comprising a gene encoding [the] a 19 kilodalton C-terminal fragment of a *Plasmodium* MSP-1 polypeptide; wherein said polynucleotide has a total GC content of 40 to 60%.

59. (Amended) The synthetic polynucleotide of Claim 56, wherein said glycosylphosphatidylinositol coding sequence is from a CD59 or CD14 gene.

62. (Amended) The synthetic polynucleotide of Claim 56 [61], wherein said synthetic polynucleotide is SEQ ID NO:9.

63. The synthetic polynucleotide of Claim 56, wherein said synthetic polynucleotide further comprises a polynucleotide encoding [the] a *Plasmodium vivax* Duffy binding protein or [the] a *Plasmodium falciparum* EBA-175 protein.

Claim 64 (Cancelled).

65. (New) A baculovirus vector comprising a promoter, a synthetic polynucleotide encoding a 19 kildalton C-terminal fragment of *Plasmodium falciparum* MSP-1 protein having a GC content of between 40% to 60% and a signal sequence from *Plasmodium vivax*.

66. (New) The baculovirus vector of Claim 65, wherein said synthetic polynucleotide sequence further comprises a glycosylphosphatidylinositol coding sequence.

67. (New) The baculovirus vector of Claim 66, wherein said glycosylphosphatidylinositol coding sequence is a CD59 or a CD14 gene.

68. (New) A baculovirus vector comprising a promoter and a synthetic nucleotide sequence comprising SEQ ID NO:7.--